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Cloning, structural analysis, and expression of the pig IgE epsilon chain.

Vernersson M, Pejler G, Kristersson T, Alving K, Hellman L.

Department of Medical Immunology and Microbiology, University of Uppsala, Sweden.

As a step in the evolutionary studies of immunoglobulin E (IgE) and for the purpose of developing new reagents that will facilitate a more detailed analysis of IgE-mediated inflammatory reactions in a large animal model, we here present the cloning of the epsilon chain of IgE in the domestic pig (*Sus scrofa*). A partial cDNA clone for the epsilon chain of pig IgE was isolated by polymerase chain reaction (PCR) amplification using degenerate primers directed against conserved regions in the second (CH2) and the fourth (CH4) constant domains of IgE. cDNA derived from mRNA isolated from the spleen and lymph nodes of a pig actively sensitized with a protein extract from the nematode *Ascaris suum* was used as template. Screening of a spleen cDNA library with the partial cDNA clone as probe resulted in isolation of a clone that contained the entire coding region. The nucleotide sequence was determined and was found to conform with the previously identified mammalian epsilon-chain sequences. The highest degree of similarity was found to sheep IgE. A DNA construct encoding a baculovirus signal sequence, a histidine hexapeptide, and the CH2-CH3-CH4 domains of the pig IgE epsilon chain was obtained by PCR amplification. The construct was ligated into the baculovirus expression vector pVL1392. Infection of High Five insect cells with recombinant baculovirus resulted in expression and secretion of a soluble 6 x His-CH2-CH3-CH4 protein product.

PMID: 9321425 [PubMed - indexed for MEDLINE]

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=> s l1 and mammalian IgE

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L3 2 DUP REMOVE L2 (1 DUPLICATE REMOVED)

=> d l3 1-2 cbib abs

L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN

2004:634150 Document No. 141:156084 Immunoglobulin E detection in mammalian species and **antibody** reagents. Hammerberg, Bruce (North Carolina State University, USA). PCT Int. Appl. WO 2004065936 A2 20040805, 14 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US3566 20040115. PRIORITY: US 2003-2003/PV440472 20030116.

AB The present invention concerns methods of detecting **mammalian IgE** (e.g., dog IgE) **antibodies** and **antibody** reagents useful therefore. In some embodiments the **antibodies** bind to an epitope between amino acids 145-166 of **mammalian IgE**; in other embodiments the **antibodies** bind to an epitope between amino acids 356-374 of **mammalian IgE**. The **antibodies** may be used for allergen reactivity testing in human subjects or animal subjects for veterinary purposes using an ELISA method.

L3 ANSWER 2 OF 2 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 1

2004:214156 The Genuine Article (R) Number: 776VT. Site-specific N-glycosylation of chicken serum IgG. Suzuki N (Reprint); Lee Y C. Johns Hopkins Univ, Dept Biol, Baltimore, MD 21218 USA (Reprint). GLYCOBIOLOGY (MAR 2004) Vol. 14, No. 3, pp. 275-292. ISSN: 0959-6658. Publisher: OXFORD UNIV PRESS INC, JOURNALS DEPT, 2001 EVANS RD, CARY, NC 27513 USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Avian serum immunoglobulin (IgG or IgY) is functionally equivalent to mammalian IgG but has one additional constant region domain (CH2) in its heavy (H) chain. In chicken IgG, each H-chain contains two potential N-glycosylation sites located on CH2 and CH3 domains. To clarify characteristics of N-glycosylation on avian IgG, we analyze N-glycans from

chicken serum IgG by derivatization with 2-aminopyridine (PA) and identified by HPLC and MALDI-TOF-MS. There were two types of N-glycans: (1) high-mannose-type oligosaccharides (monoglucosylated 26.8%, others 10.5%) and (2) biantennary complex-type oligosaccharides (neutral, 29.9%; monosialyl, 29.3%; disialyl, 3.7%) on molar basis of total N-glycans. To investigate the site-specific localization of different N-glycans, chicken serum IgG was digested with papain and separated into Fab [containing variable regions (VH + VL) + CH1 + CL] and Fc (containing CH3 + CH4) fragments. Con A stained only Fc (CH3 + CH4) and RCA-I stained only Fab fractions, suggesting that high-mannose-type oligosaccharides were located on Fc (CH3 + CH4) fragments, and variable regions of Fab contains complex-type N-glycans. MS analysis of chicken IgG-glycopeptides revealed that chicken CH3 domain (structurally equivalent to mammalian CH2 domain) contained only high-mannose-type oligosaccharides, whereas chicken CH2 domain contained only complex-type N-glycans. The N-glycosylation pattern on avian IgG is more analogous to that in **mammalian IgE** than IgG, presumably reflecting the structural similarity to **mammalian IgE**.

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=> s L1 and IgE
L4      58972 L1 AND IGE
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=> s l4 and canine IgE
L5      95 L4 AND CANINE IGE
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=> s l5 and anti-IgE
L6      25 L5 AND ANTI-IGE
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L7      10 DUP REMOVE L6 (15 DUPLICATES REMOVED)
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L7      ANSWER 1 OF 10      MEDLINE on STN      DUPLICATE 1
2002269908.      PubMed ID: 12013481.      Evaluation of cell-surface IgE
receptors on the canine mastocytoma cell line C2 maintained in continuous
culture. Brazis Pilar; Torres Rosa; Queralt Mireia; de Mora Fernando;
Ferrer Lluís; Puigdemont Anna. (Departament de Farmacologia, Facultat de
Veterinària, Universitat Autònoma de Barcelona, Spain. ) American journal
of veterinary research, (2002 May) 63 (5) 763-6. Journal code: 0375011.
ISSN: 0002-9645. Pub. country: United States. Language: English.
AB      OBJECTIVE: To assess expression and function of cell-surface IgE
receptors on the canine mastocytoma cell line C2 maintained in continuous
culture. SAMPLE POPULATION: C2 cells maintained in medium lacking
IgE for up to 10 passages before being stored at -80 C.
PROCEDURE: Cells were thawed, cultured in medium without IgE for
1 to 3 passages, sensitized for 7 days with IgE-rich serum from
dogs naturally sensitized to Ascaris suum, and stimulated with antigen Asc
S1 from A. suum, goat polyclonal anti-canine IgE, or
calcium ionophore and phorbol myristate acetate (PMA). Percentage of
intracellular beta-hexosaminidase released and concentration of tumor
necrosis factor-alpha (TNF-alpha) synthesized after stimulation were
determined. Expression of cell-surface IgE receptors was
assessed by use of a flow cytometry. RESULTS: Immunologic stimulation
(antigen or anti-IgE) failed to induce release or
synthesis of detectable amounts of beta-hexosaminidase or TNF-alpha. In
contrast, nonimmunologic stimulation (calcium ionophore and PMA) led to
release of beta-hexosaminidase (mean +/- SEM maximum release,
23.95+/-1.96%) and synthesis of TNF-alpha (maximum concentration,
34.34+/-2.34 pg/10(6) cells). As revealed by use of flow cytometry, C2
cells expressed surface IgE receptors that bound canine
IgE in vitro. CONCLUSIONS: Continuous culture of the canine
mastocytoma cell line C2 in medium without exogenous IgE or
```

cytokines and other growth factors resulted in cell-surface expression of nonfunctional **IgE** receptors. However, C2 cells maintained in continuous culture may still be a useful tool for the evaluation of mast cell responses to nonimmunologic stimulation and **IgE** receptor differentiation and maturity.

- L7 ANSWER 2 OF 10 MEDLINE on STN DUPLICATE 2
2002720815. PubMed ID: 12483035. IgG-mediated signal transduction in canine mastocytoma-derived cells. Sato Yoshitaka; Teshima Reiko; Nakamura Ryosuke; Sasaki Nobuo; Morita Yutaka; Sawada Jun-ichi; Kitani Seiichi. (Department of Respiratory Medicine, Graduate School of Medicine, University of Tokyo, Japan.) International archives of allergy and immunology, (2002 Dec) 129 (4) 305-13. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.
- AB BACKGROUND: We have reported canine cutaneous mastocytoma-derived cells named CM-MC sensitized with monomeric IgG released histamine upon anti-IgG stimulation. However, IgG or **IgE**-mediated signal transduction in the cells remains to be examined. METHODS: Monomeric IgG-binding to cells was measured by flow cytometry using FITC-anti-IgG. IgG-mediated protein tyrosine phosphorylation was studied by Western blotting using anti-phosphotyrosine **antibody**. We monitored the intracellular Ca(2+) concentration ([Ca(2+)](i)) when IgG-primed cells were activated with anti-canine IgG. Release of Ca(2+) from intracellular stores was analyzed with thapsigargin in the absence of extracellular Ca(2+). The Ca(2+) entry via store-operated Ca(2+) channel from the external environment was characterized using Ba(2+), Ni(2+) and EGTA. Cells sensitized with canine serum abundant in IgG and **IgE** or heat-inactivated serum were activated by anti-canine IgG or anti-**canine IgE**. The effect of extracellular Ca(2+) and reaction time on IgG-mediated histamine release was examined. Staurosporine and ER-27319 were used to clarify the IgG-mediated protein tyrosine phosphorylation. RESULTS: Abundant IgG-binding sites on the cell were detected by FACS analysis. Anti-IgG induced rapid protein tyrosine phosphorylation and [Ca(2+)](i) elevation. When extracellular Ca(2+) was excluded by EGTA, a mild and transient increase in [Ca(2+)](i) was observed, indicating the release of Ca(2+) from anti-IgG-sensitive intracellular Ca(2+) stores. The constant Ba(2+) entry from external environment proved the Ca(2+) influx occurred mainly via a store-operated Ca(2+) channel which was inhibited by Ni(2+) and EGTA. Canine serum-sensitized cells showed a rapid and sustained increase in [Ca(2+)](i) upon both anti-IgG and **anti-IgE** stimulation. The [Ca(2+)](i) elevation induced by **anti-IgE** was decreased in the cells sensitized with heat-inactivated serum. Histamine release from CM-MCs was absolutely dependent on extracellular Ca(2+), and reached equilibrium within 5 min. Staurosporine inhibited the tyrosine phosphorylation of 38-, 65-, 70-, 80-kD proteins. ER-27319 inhibited the tyrosine phosphorylation of 38- and 70-kD proteins. Staurosporine also inhibited IgG-mediated [Ca(2+)](i) elevation and histamine release in a dose-dependent manner. CONCLUSIONS: Canine cutaneous mastocytoma-derived (CM-MC) cells were activated by both IgG- and **IgE**-mediated mechanisms. IgG-mediated protein tyrosine phosphorylation and Ca(2+) influx were similar to those mediated by **IgE**. CM-MC cells are useful for the study of allergic inflammation caused by IgG-dependent mechanisms.
Copyright 2002 S. Karger AG, Basel
- L7 ANSWER 3 OF 10 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
2002:429597 The Genuine Article (R) Number: 551HW. **IgE** is present on peripheral blood monocytes and B cells in normal dogs and dogs with atopic dermatitis but there is no correlation with serum **IgE** concentrations. Jackson H A (Reprint); Orton S M; Hammerberg B. N Carolina State Univ, Comparat Allergy Program, 4700 Hillsborough St, Raleigh, NC 27606 USA (Reprint); N Carolina State Univ, Comparat Allergy Program, Raleigh, NC 27606 USA. VETERINARY IMMUNOLOGY AND IMMUNOPATHOLOGY

(MAR 2002) Vol. 85, No. 3-4, pp. 225-232. ISSN: 0165-2427. Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB

Blood was collected from 29 dogs, 14 with atopic dermatitis (AD) and 15 controls. Total serum **IgE** was quantitated. Peripheral blood monocytes were harvested and labeled with leucocyte markers and anti-**canine IgE** before analysis by flow cytometry. There was no statistically significant difference between the atopic and control groups when the mean number of cells in the monocyte (CD14), antigen presenting cell (CD1c) or B cell (CD21) populations were examined. However, the variation in cell numbers was significant and much greater in the atopic group for CD1c and CD14 labeled cells. The mean percentage of double labeled cells, CD1c/**IgE** and CD14/**IgE** was significantly lower in the atopic population compared with the controls. More variation was observed in the numbers of monocytes of atopic dogs (CD14/**IgE**) and antigen presenting cells (CD1c/**IgE**) of control dogs. The mean percentage of B cells expressing **IgE** was 65 and 51% in the atopic and control groups respectively which is greater than that reported in humans. There was no statistically significant difference. Total serum **IgE** concentrations were similar in each group and did not correlate with cell bound **IgE** in any of the leucocyte populations studied. Canine AD is associated with more variability in circulating monocyte numbers and lower numbers of monocytes expressing **IgE** than control dogs. Unlike in humans, there is no correlation between circulating and cell bound **IgE**. Furthermore, high levels of **IgE** in the dog may be related to a greater number of B cells in the circulation committed to **IgE** production. (C) 2002 Published by Elsevier Science B.V.

L7 ANSWER 4 OF 10 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

2001:200942 The Genuine Article (R) Number: 405RE. Naturally occurring **canine IgE anti-IgE** that binds **IgE**-bearing B cells butnot**IgE** bound to mast cells, isolated as a canine monoclonal **antibody** from a canine X mouse heterohybridoma . Hammerberg B (Reprint); Simkins S; Orton S M. N Carolina State Univ, Raleigh, NC 27695 USA. JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY (FEB 2001) Vol. 107, No. 2, Supp. [S], pp. S272-S272. MA 889. ISSN: 0091-6749. Publisher: MOSBY, INC, 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO 63146-3318 USA. Language: English.

L7 ANSWER 5 OF 10 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

1998:491185 The Genuine Article (R) Number: ZU926. Canine atopic dermatitis - pathomechanisms and comparison of ICT and ELISA with monoclonal **anti-IgE-antibody**. Hammerling R (Reprint); Leidinger K. Spichernstr 8, D-40476 Dusseldorf, Germany (Reprint); Tierarztl Praxis Kleine Haustiere Spichernpl, Dusseldorf, Germany; Labors Biocontrol, Vet Med Abt, Mainz, Germany. PRAKTISCHE TIERARZT (1 JUN 1998) Vol. 79, No. 6, pp. 509-+. ISSN: 0032-681X. Publisher: SCHLUTERSCHE VERLAG DRUCKEREI, GEORGSWALL 4, W-3000 HANOVER 1, GERMANY. Language: German.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB

Atopic dermatitis in the dog is caused by a complex of humoral and cellular immunological dysregulations. A lot of research was done by many investigators regarding not only the clinical signs but also the pathomechanisms, which are very important for the symptoms and the interpretation of the results of the different allergy test systems. The following investigation was performed to compare the results of an ELISA and the I.c.-test prepared with allergens from the same company. After excluding other pruritic diseases in 90 dogs with suspected atopic dermatitis allergy tests were performed simultaneously with an ELISA based on a monoclonal anti-**canine-IgE antibody** and intradermal skin tests with allergens from GREER(1) and imovet bg(2). With the pollens from grasses, weeds and trees the ELISA showed more

positive reactions than the skin test, even when performed in wintertime. Nevertheless the reaction against pollens were very rare, even when the tests were done in spring and summer, so pollens in our region are mostly not the reason for atopic dermatitis in dogs. Most of the dogs with atopic dermatitis reacted against mites, first of all against *D. farinae*, somewhat less against *D. pteronyssinus*, but as often against storage mites, especially against *Acarus siro*. Further studies will show whether these reactions are really positive in fact by hypersensitivity or only caused by crossreactivity. With an elimination-diet based on meat and potatoes the clinical symptoms mostly resolved. Between the ELISA and the different allergens in the skin test there were only very few concords even with the mites. The large number of positive reactions in the skin test with *Alternaria* from imovet bg(2) was considered to be false positive. The results of the skin test and the ELISA have to be considered very carefully together with the history and clinical symptoms. For specific immunotherapy it is important to estimate the test results under knowledge of the used allergens and the ELISA. The use of fractionated allergens and a cocktail of monoclonal anti-canine-IgE-antibodies may improve the results.

L7 ANSWER 6 OF 10 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

1998:762132 The Genuine Article (R) Number: 123EA. Passive **antibody** transfer on human leukocytes: application to small animal allergy diagnosis by flow cytometry. Sainte-Laudy J (Reprint). Lab Cerba, Unite Immunoallergol, Val Doise 09, France (Reprint). VETERINARY DERMATOLOGY (SEP 1998) Vol. 9, No. 3, pp. 207-211. ISSN: 0959-4493. Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 ONE, OXON, ENGLAND. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Animal allergy diagnosis is based mainly on clinical history, skin tests and, at least for dogs, specific **IgE antibodies**. The quality of anti-canine **IgE antibodies** is variable and monoclonal **antibodies** have been recently characterized. The allergen panel tested in humans and in dogs is similar except for flea and for *Staphylococcus*. Allergen-induced basophil activation may be measured by the release of mediators such as histamine and leukotriene C4 and by the expression of the CD63 marker on basophil membrane. This latter method is based on the flow cytometric analysis of leukocyte suspensions after double **anti-IgE FITC**, anti-CD63 PE labelling of human basophils, and has been validated for aero-allergens, food allergens, venoms and several drugs for human allergy diagnosis. After having demonstrated that, in the dog, anaphylactic **antibodies** were capable of binding to human basophil high-affinity receptors for **IgE**, we went up a flow cytometric method for animal allergy diagnosis based on passive sensitization of human basophils. Preliminary results obtained by this method for allergens such as house dust mite or pollen were very encouraging. This method is faster and less expensive than the methods based on mediator release but is still dependent on the availability of fresh human leukocytes. This method may represent a new sensitive and specific method for animal allergy diagnosis.

=> s l4 and cat IgE

L8 14 L4 AND CAT IGE

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L9 7 DUP REMOVE L8 (7 DUPLICATES REMOVED)

=> d l9 1-7 cbib abs

L9 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

2003:42915 Document No. 138:88663 Feline **IgE**. McCall, Catherine;

Weber, Eric (USA). U.S. Pat. Appl. Publ. US 2003013183 A1 20030116, 45 pp. (English). CODEN: USXXCO. APPLICATION: US 2000-479614 20000107. PRIORITY: US 1999-PV115033 19990107.

AB The authors disclose cloning and sequence characterization for a light chain and heavy chains of feline **IgE**. In addition, the authors disclose the preparation of mouse monoclonal **antibodies** that recognize feline **IgE** and/or light chain.

L9 ANSWER 2 OF 7 MEDLINE on STN DUPLICATE 1

2003395122. PubMed ID: 12931642. Epidemic study of pet allergy in Wakayama Prefecture. Seno Satoshi; Enomoto Tadao; Dake Yoshihiro; Saito Yuko; Ikeda Hiroki; Funakoshi Hiroko; Sogo Hideyo; Shibano Akira; Sakota Takema; Suzuki Mikio; Yazawa Yoshiro. (Department of Otolaryngology, Head & Neck Surgery, Shiga University of Medical Science, Otsu.) Nippon Jibiinkoka Gakkai kaiho, (2003 Jul) 106 (7) 750-3. Journal code: 7505728. ISSN: 0030-6622. Pub. country: Japan. Language: Japanese.

AB In Japan, the number of households who have pets has gradually increased, together with the number of people who have pet allergies. Many reports exist on pollen and mite allergy, but few on pet allergy. We conducted an epidemic study in 531 first-year junior high school students in Wakayama prefecture in 1999. Questionnaires covered allergy and measurement of total **IgE antibody** using CAP system (Pharmacia Co. Ltd.) and specific **IgE antibody** using MAST26 system (Hitachi chemical Co. Ltd.). Of 306 students having pets, 11 were allergic to dogs, 11 to cats, 8 to both, and 1 to rabbits. Clinical symptoms were various. No differences in symptoms were observed among allergens. Serum total **IgE** tended to increase in students who suffered from pet allergies. Positive rates of specific **IgE antibodies** were high in mites and Japanese cedar pollen (36.7% for mites and 37.0% for Japanese cedar pollen), and also in dogs and cats (15.4% for dogs and 18.2% for cats). Specific dog and cat **IgE antibodies** increased significantly ($p = 0.033$ for dog and for $p < 0.0001$ cat), but no significant correlation was found between the positive specific **IgE antibody** and history of pet keeping.

L9 ANSWER 3 OF 7 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

1998:612239 The Genuine Article (R) Number: 108PE. Quantitation of cat immunoglobulins in the hemolymph of cat fleas (Siphonaptera : Pulicidae) after feeding on blood. Vaughan J A (Reprint); Thomas R E; Silver G M; Wisniewski N; Azad A F. Univ Maryland, Sch Med, Dept Microbiol & Immunol, Baltimore, MD 21201 USA (Reprint). JOURNAL OF MEDICAL ENTOMOLOGY (JUL 1998) Vol. 35, No. 4, pp. 404-409. ISSN: 0022-2585. Publisher: ENTOMOL SOC AMER, 9301 ANNAPOLIS RD, LANHAM, MD 20706 USA. Language: English. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Passage of ingested cat immunoglobulin G (IgG) into the hemocoel of cat fleas, *Ctenocephalides felis* (Bouche), was examined using **antibody** capture enzyme-linked immunosorbent assays (ELISA) and Western blotting. Fleas were fed heparinized cat blood via membrane feeders. Cat **IgG** was present in the hemolymph of engorged female fleas 1 h after ingestion at an estimated quantity of $35 \pm 14 \mu\text{g/ml}$. The prevalence of fleas with demonstrable cat IgG in their hemolymph 1 h after feeding was 100% for both female and male fleas. Following a single blood meal, cat IgG was present in the hemolymph of all 15 fleas tested 1 h after ingestion but dissipated below detectable levels in 10 of 20 fleas examined 3 h after ingestion, and was detectable in only 1 of 10 fleas examined 18 h after ingestion. However, when fleas were provided with continual access to blood over a 72-h period. IgG content in hemolymph, as measured in excised, triturated legs of individual fleas, remained fairly constant (3-16 pg IgG per sample). Flea feeding studies using specific antisera indicated that IgG in flea hemolymph retained its binding activity, and that at least a portion of the IgG was intact. Passage of ingested host **antibody** from gut into hemocoel is a prerequisite for the possible development of antiflea vaccines that target

antigens outside of the flea midgut lumen (e.g., key components of the nea endocrine system controlling oogenesis).

L9 ANSWER 4 OF 7 MEDLINE on STN DUPLICATE 2
97265593. PubMed ID: 9111499. Rush immunotherapy results in allergen-specific alterations in lymphocyte function and interferon-gamma production in CD4+ T cells. Lack G; Nelson H S; Amran D; Oshiba A; Jung T; Bradley K L; Giclas P C; Gelfand E W. (Department of Pediatrics, National Jewish Center for Immunology and Respiratory Medicine, Denver, Colorado 80206, USA.) Journal of allergy and clinical immunology, (1997 Apr) 99 (4) 530-8. Journal code: 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB BACKGROUND: Allergen immunotherapy results in a number of changes in clinical, inflammatory, and immunologic parameters. However, the basis for the specificity of this form of therapy is unknown, especially in the context of changes in T- and B-lymphocyte function after desensitization to specific allergens. OBJECTIVE: This study was designed to determine the immunologic consequences of rush immunotherapy. METHODS: We studied 10 patients who had positive skin test responses to the house dust mite *Dermatophagoides pteronyssinus* (Dpt) and cat dander extract. Each received rush immunotherapy to mite, but not cat dander, over a 2- to 4-week period until maintenance was achieved. Patients were evaluated before and when maintenance was achieved for skin test and nasal reactivity to mite and cat dander; **antibody** levels to the allergen were monitored, as were lymphocyte proliferative responses and cytokine production. RESULTS: Rush immunotherapy to house dust mite resulted in a significant reduction in skin and nasal reactivity to mite allergen, but not to cat allergen, in 10 of 10 patients. This was accompanied by a rise in serum anti-Dpt **IgE**, whereas anti-**cat IgE** was not altered (7 of 7 patients). In seven of seven patients there was an increase in anti-Dpt **IgG4** levels. T-cell proliferative responses to mite antigen were suppressed, and numbers of CD8+ T cells increased in frequency. There was a marked increase in interferon-gamma production, particularly by CD4+ T cells in 10 of 10 patients. The correlation between the increases in interferon-gamma production and the changes in cutaneous reactivity was highly significant. CONCLUSION: We show that rush immunotherapy is immunologically specific in eliciting changes in T- and B-cell responses to the desensitization antigen. The specificity and potential benefit of immunotherapy may be linked to the increase in interferon-gamma production by allergen-activated CD4+ T lymphocytes.

L9 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
1995:806474 Document No. 123:196608 Epitope of feline **IgE** present on feline B-cell but not basophil cell surfaces and its use in allergy therapy and diagnosis. Chang, Tse Wen (Tanox Biosystems, Inc., USA). PCT Int. Appl. WO 9515977 A1 19950615, 25 pp. DESIGNATED STATES: W: AT, AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1994-US14407 19941206. PRIORITY: US 1993-164910 19931209.

AB Antigenic epitopes associated with the extracellular segment of the domain which anchors Igs to the feline B cell membrane are disclosed. For **IgE**, the epitopes are present on **IgE**-bearing B cells but not basophils or the secreted, soluble form of **IgE**. The epitope can be exploited for therapy and diagnosis. For example, peptides representing the epitopes associated with the anchor domain of **IgE** can be used to generate **antibodies** against these regions, for use in cat allergy therapy and anal. of **cat IgE**-bearing B lymphocytes.

L9 ANSWER 6 OF 7 MEDLINE on STN DUPLICATE 3
90131528. PubMed ID: 2299111. Variability of cat-allergen shedding. Wentz P E; Swanson M C; Reed C E. (Mayo Clinic, Rochester, Minn 55905.) Journal

of allergy and clinical immunology, (1990 Jan) 85 (1 Pt 1) 94-8. Journal code: 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB To study the differences in total allergen shed, nine cats were placed individually in a lucite chamber with an air sampler attached for 1 hour. With a RAST-inhibition assay that used specific **cat IgE antibodies** from cat-sensitive subjects, we ranked the allergen production of each cat. From these nine cats, three high producers and one low producer were studied further. Each cat's allergens were collected for two to four separate 1-hour intervals on 6 different days. The high producers' samples remained high in allergen content, and the low producer's sample remained low. An additional eight cats were selected for similar longitudinal measurements, and allergens from each of these 12 cats were collected during four 1-hour intervals on 2 different days and assayed for total allergy units (AUs) by RAST inhibition and for the major cat allergen, Fel d I, by a two-site assay with a monoclonal **antibody**. Shedding, particularly by high producers, varied considerably from hour to hour. We found a hundredfold difference in AUs between the mean rate of shedding of the highest and lowest producers and a sixfold difference in Fel d I units. Variation in rate of shedding of Fel d I accounted for about half the variation of shedding of AUs. Allergen shedding varies not only between cats but also in the same cat during the course of a day and between days. Male cats shed more than female cats.

L9 ANSWER 7 OF 7 MEDLINE on-STN DUPLICATE 4
89080064. PubMed ID: 2462581. Immunotherapy for cat asthma. Van Metre T E Jr; Marsh D G; Adkinson N F Jr; Kagey-Sobotka A; Khattignavong A; Norman P S Jr; Rosenberg G L. (Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD.) Journal of allergy and clinical immunology, (1988 Dec) 82 (6) 1055-68. Journal code: 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB In 22 patients with cat asthma who were highly sensitive to cat, we compared, double-blind, the effects of immunotherapy with cat-hair and dander extract (11 patients) with effects of placebo (11 patients). Patients were matched by the dose of the cat extract expressed in Food and Drug Administration (FDA) units of Fel d I (previously called cat allergen 1) required for end point reaction in intradermal skin test end point titration (STEPT), for in vitro leukocyte histamine release (LHR), and for the dose of cat extract producing a 20% fall in FEV1 (cat-extract PD20) in bronchoprovocation test. Patients were matched also for bronchoprovocation dose of methacholine producing a 20% fall in FEV1 (methacholine PD20). Patients were randomly assigned to one of two treatment groups. During immunotherapy, doses were increased to maintenance dose of 4.56 FDA units of Fel d I, or, if this were less, to the highest tolerated dose. Systemic reactions to cat-extract immunotherapy were mild and infrequent. Before and during immunotherapy, we measured (in FDA units of Fel d I) cat-extract PD20, cat-extract intradermal STEPT, cat-extract in vitro LHR, serum levels of cat IgG and **cat IgE**, and methacholine PD20. After they had received 1 year of immunotherapy, patients receiving cat extract, in comparison to patients receiving placebo, had decreased cat-extract PD20 (p less than 0.01), diminished responses to cat-extract intradermal STEPT (p less than 0.025), increased **IgE antibodies** toward cat extract (p less than 0.01), increased IgG **antibodies** toward cat extract, Fel d I, and cat albumin (p less than 0.001), but no significant change in cat-extract in vitro LHR or in methacholine PD20. We conclude that cat-extract immunotherapy was well tolerated, significantly decreased skin and bronchial responses to cat extract, and significantly increased **IgE antibodies** to cat extract and IgG **antibodies** to cat extract, Fel d I, and cat albumin.

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PROCESSING COMPLETED FOR L10

L11 7 DUP REMOVE L10 (7 DUPLICATES REMOVED)

=> d l11 1-7 cbib abs

L11 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

2003:355731 Document No. 138:336418 Heavy chain derived peptides for induction of anti-IgE antibodies. Gershwin, Laurel J.; Pettigrew, Howard David; Kalina, Warren V. (The Regents of the University of California, USA). U.S. Pat. Appl. Publ. US 2003087314 A1 20030508, 14 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-52788 20011108.

AB The present invention relates to identification of polypeptides useful for generating antibodies specific for non-human IgE, particularly equine IgE. The invention, therefore, also relates to antibodies that specifically bind to IgE and methods to detect IgE using the antibodies. The invention also provides a kit for detection of IgE.

L11 ANSWER 2 OF 7 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 1

2003:288496 The Genuine Article (R) Number: 659CC. Monoclonal anti-equine IgE antibodies with specificity for different epitopes on the immunoglobulin heavy chain of native IgE. Wagner B (Reprint); Radbruch A; Rohwer J; Leibold W. Cornell Univ, Coll Vet Med, Inst Anim Hlth, Hungerford Hill Rd, Ithaca, NY 14853 USA (Reprint); Hannover Sch Vet Med, Immunol Unit, D-30173 Hannover, Germany; German Rheumatism Res Ctr, D-10117 Berlin, Germany. bw73@cornell.edu. VETERINARY IMMUNOLOGY AND IMMUNOPATHOLOGY (20 MAR 2003) Vol. 92, No. 1-2, pp. 45-60. ISSN: 0165-2427. Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In this study we describe the generation of monoclonal antibodies (mAbs), which recognize different epitopes of the equine IgE constant heavy chain. Equi-murine recombinant IgE (rIgE), composed of the murine V-H 186.2 heavy chain variable region, linked to the equine IgE constant heavy chain and expressed together with the murine lambda(1) chain in J558L cells was used to immunize BALB/C mice. A total of 17 different mAbs were obtained, which recognized the rIgE heavy chain constant region. None of the mAbs reacted with monoclonal equine isotypes IgM, IgG1 (IgGa), IgG3 (IgG(T)), IgG4 (IgGb) or isolated equine light chains, IgGc and IgA from horse serum, or the native mAb B1-8delta, expressing the same heavy chain variable regions and light chains. One of the mAbs (alphaIgE-132) recognized the recombinant equine IgE, but did not recognize any protein in equine serum, i.e. native IgE. A total of 16 mAbs detected a serum protein of approximately 210,000 Da on Western blots, corresponding to the expected MW of native IgE. In addition, one of the mAbs (alphaIgE-176) detected a protein of 76,000 Da under reducing conditions, most likely the equine IgE heavy chain. According to binding inhibition studies, the equine IgE specific mAbs recognize at least two different epitopes of the equine IgE. In an ELISA using two anti-IgE mAbs which recognized different epitopes, no significant differences in the concentration of total serum IgE could be detected between adult Icelandic horses with IgE-mediated type I allergy (summer eczema) and healthy control animals. In Icelandic horse foals, no serum IgE could be measured 6 months post partum. All anti-IgE mAbs recognized a small population (1.3 +/- 0.5%) of leukocytes from adult Icelandic horses by surface immunofluorescence, but no cells could be detected in foal blood. The stained leukocytes from adult horses could be enriched by magnetic cell sorting and contained 32% basophils, 53% monocytes and/or large lymphocytes, 13% small lymphocytes and 2% eosinophils. (C) 2003

L11 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

2002:487751 Document No. 137:62173 Genes for the **horse IgE**
-allotype heavy chain constant region for use in the construction of
chimeric **antibodies** and isotype-specific monoclonal
antibodies. Leibold, Wolfgang; Wagner, Bettina; Radbruch, Andreas
(Tierärztliche Hochschule Hannover, Germany). PCT Int. Appl. WO
2002050280 A2 20020627, 37 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT,
AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM,
DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,
MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF,
CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML,
MR, NE, NL, PT, SE, SN, TD, TG, TR. (German). CODEN: PIXXD2.
APPLICATION: WO 2001-DE4810 20011220. PRIORITY: DE 2000-10064415
20001221.

AB The invention relates to novel equine C α and C ϵ genes
for **IgE** allotype heavy chain constant regions and used in the
production of **IgE**-isotype recombinant Ig. Said recombinant Igs
represent valuable auxiliary agents for **IgE**-diagnosis, especially
equine allergy diagnosis. With the aid of the recombinant **IgEs**,
antibodies are obtained that can be used in allergy diagnosis,
inter alia, in ELISA-based test kits. cDNAs were cloned by PCR using
primers derived from known **horse IgE** heavy chain
constant regions. The cDNA was used to construct a gene for a fusion
protein of a horse heavy chain constant region and a mouse heavy chain
variable region and the gene expressed in J558L myeloma cells where it
formed an **antibody** with λ chains elaborated by the cell.
The preparation of monoclonal **antibodies** to the **IgE** heavy
chain and use of the **antibodies** are described.

L11 ANSWER 4 OF 7 MEDLINE on STN DUPLICATE 2

1998137963. PubMed ID: 9477476. Chicken **antibodies** to a
recombinant fragment of the equine immunoglobulin epsilon heavy-chain
recognising native **horse IgE**. Marti E; Peveri P;
Griot-Wenk M; Muntwyler J; Cramer R; Schaller J; Gerber H; Lazary S.
(Klinik für Nutztiere und Pferde, University of Berne, Switzerland..
marti@itz.unibe.ch). Veterinary immunology and immunopathology, (1997
Nov) 59 (3-4) 253-70. Journal code: 8002006. ISSN: 0165-2427. Pub.
country: Netherlands. Language: English.

AB An equine immunoglobulin E (**IgE**) heavy-chain cDNA fragment
(CH3-CH4, nucleotides 1132 to 1592) was cloned, expressed in *Escherichia*
coli as a fusion protein with a [His]6-tag and purified over a Ni-NTA
column. The recombinant protein was used to immunise hens. Testing of
the raised egg yolk immunoglobulin G (**IgG**) in Western-blot and ELISA
revealed high titres against the recombinant equine **IgE** fragment
(reqIgEf). The reqIgEf-specific **IgG** was successfully affinity-purified on
an unconventional affinity matrix: the [His]6-tagged recombinant
IgE fragment was bound to Ni-NTA agarose and used to adsorb
specific immunoglobulins. In Western-blot of ammonium sulphate
precipitated horse serum and bronchoalveolar lavage fluid, separated by
SDS-PAGE under denaturing-reducing conditions, the raised
antibodies reacted with a protein of approximately 80 kDa. A
reaction of the reqIgEf-specific **IgG** was seen with a 190-200 kDa band when
the same horse serum or bronchoalveolar fluid (BALF) was separated under
non-reducing conditions. These reactions could be inhibited by
preincubation of the immune **IgG** with reqIgEf, while preincubation with
horse **IgG** did not inhibit the reaction. **Antibody**-affinity
chromatography of horse serum with the reqIgEf-specific chicken **IgG**
resulted in an enrichment of the 80 kDa protein in denaturing
Western-blot. Determination of the amino acid composition of this protein
and comparison with the equine **IgE** heavy-chain sequence
strongly indicates that the 80 kDa band corresponds to the heavy chain of

the horse IgE. The reqIgEf-specific chicken IgG was further characterised in an ELISA for the detection of allergen-specific horse IgE. It was demonstrated that heating IgE positive horse sera at 54 degrees C for 10 min drastically diminished the recognition by the reqIgEf-specific chicken IgG. The reaction is inhibitable by preincubation with reqIgEf in a concentration dependent manner. In addition, preincubation with horse IgG, a nonrelevant [His]6-tagged protein or 2% equine colostrum had no influence on the reqIgEf-specific chicken IgG binding characteristic. This antibody recognising horse IgE will be useful for further studies on the pathogenesis of equine allergic diseases.

L11 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

1994:473887 Document No. 121:73887 Method and composition using allergen and substance P for treating IgE-mediated allergies. Patterson, Roy; Harris, Kathleen E. (Northwestern University, USA). U.S. US 5314690 A 19940524, 23 pp. Cont.-in-part of U.S. Ser. No. 705,071, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1992-934553 19920821. PRIORITY: US 1991-705071 19910524.

AB The present invention relates to a method and prepns. for reducing IgE antibodies to allergens in allergic subjects, in which substance P and an allergen, or fragments of allergens or haptens acting as allergens, are administered together to the allergic subjects. The method can be used to treat humans and animals including dogs, cats, horses and subhuman primates. Cutaneous titer to rye grass antigen in a human subject is reported; the subject was treated with rye grass allergen and substance P. Studies of monkeys treated with Ascaris antigen and substance P are also reported.

L11 ANSWER 6 OF 7 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

88176428 EMBASE Document No.: 1988176428. Detection of anti-horse serum antibody produced by injecting an antivenin or antitoxin (Report 2). Ameno S.; Ameno K.; Fuke C.; Kiryu T.; Sogo K.; Yodoya J.; Ijiri I.; Tsunenari S.. Department of Forensic Medicine, Kumamoto University Medical School, Kumamoto 860, Japan. Japanese Journal of Legal Medicine Vol. 42, No. 2, pp. 161-168 1988.

ISSN: 0047-1887. CODEN: NHOZAX

Pub. Country: Japan. Language: Japanese. Summary Language: English.

ED Entered STN: 911211

AB For a study involving the immunological pathogenesis of anaphylactic shock due to an injection of Mamushi antivenin or tetanus antitoxin, the anti-horse serum antibodies of the IgG and IgE class have been examined by ELISA methods in patients who had sustained a snake bite by a Japanese Mamushi (Agkistrodon halys blomhoffi BOIE) or injuries requiring a tetanus antitoxin. We were able to observe 22 patients who had received a single shot of Mamushi antivenin and no anti-horse IgG antibody was detected in their sera at about 1 week after receiving the injection, though IgG antibodies of 10-103 titers were detected at about 2 weeks. These antibodies also were detected at one, three, five, and six years after injection. An anti-horse IgE antibody was detected in only two patients who both had an anti-horse IgG antibody of high titers. In one patient, who had been injected with a Mamushi antivenin twice, 6 years ago and at this time, the respective antibody titers of anti-horse IgG and IgE antibodies were 105-104 and 104-10 during 8 to 40 days after the second injection. In patients who had been injected with tetanus antitoxins, no anti-horse IgG and IgE antibodies were detected at 1 week after injection. The IgG antibody of 10-102 titers was detected in 8 out of 15 patients, and of 104 titers in one patient, and was not detected in 6 patients at 1 month after the injection, whereas the anti-horse IgE antibody of 10 titers was detected in 6 patients, and of 102 titers in one patient and of 103 titers in another patient, and not detected in 7 patients. In one patient, who manifested symptoms due

to an allergic reaction, the titers of the anti-horse IgG antibody were 104 and those of the anti-horse IgE antibody were 103, respectively.

L11 ANSWER 7 OF 7 MEDLINE on STN DUPLICATE 3
83303750. PubMed ID: 6612985. Further purification and characterisation of horse IgE. Suter M; Fey H. Veterinary immunology and immunopathology, (1983 Jul) 4 (5-6) 545-53. Journal code: 8002006. ISSN: 0165-2427. Pub. country: Netherlands. Language: English.

AB Horse IgE was isolated from a serum pool collected from foals naturally infected with endoparasites. The serum was precipitated with ammonium sulfate, delipidated with dextran sulfate and further purified by gel filtration, anionic exchange, immunosorption or preparative polyacrylamide gelelectrophoresis. By these methods IgE could be isolated at a purity of 81%. The sera from rabbits immunized with the purified horse serum fractions were tested using reversed passive cutaneous anaphylaxis and an enzyme linked immunosorbent assay (ELISA). By the ELISA method cross reaction of rabbit anti horse IgE sera to human, mouse and rat myeloma IgE was demonstrated. Rat myeloma IgE also served to monitor the production of antibodies to horse IgE in rabbits.

=> s l4 and 356-374

L12 1 L4 AND 356-374

=> d l12 chib abs

L12 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
2004:634150 Document No. 141:156084 Immunoglobulin E detection in mammalian species and antibody reagents. Hammerberg, Bruce (North Carolina State University, USA). PCT Int. Appl. WO 2004065936 A2 20040805, 14 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US3566 20040115. PRIORITY: US 2003-2003/PV440472 20030116.

AB The present invention concerns methods of detecting mammalian IgE (e.g., dog IgE) antibodies and antibody reagents useful therefore. In some embodiments the antibodies bind to an epitope between amino acids 145-166 of mammalian IgE; in other embodiments the antibodies bind to an epitope between amino acids 356-374 of mammalian IgE. The antibodies may be used for allergen reactivity testing in human subjects or animal subjects for veterinary purposes using an ELISA method.

=> s l4 and 145-166

L13 1 L4 AND 145-166

=> d l13 chib abs

L13 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
2004:634150 Document No. 141:156084 Immunoglobulin E detection in mammalian species and antibody reagents. Hammerberg, Bruce (North Carolina State University, USA). PCT Int. Appl. WO 2004065936 A2 20040805, 14 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KZ, KZ, LC,

LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US3566 20040115. PRIORITY: US 2003-2003/PV440472 20030116.

AB The present invention concerns methods of detecting mammalian **IgE** (e.g., dog **IgE**) **antibodies** and **antibody** reagents useful therefore. In some embodiments the **antibodies** bind to an epitope between amino acids 145-166 of mammalian **IgE**; in other embodiments the **antibodies** bind to an epitope between amino acids 356-374 of mammalian **IgE**. The **antibodies** may be used for allergen reactivity testing in human subjects or animal subjects for veterinary purposes using an ELISA method.

=> s (hammerberg b?/au)
L14 196 (HAMMERBERG B?/AU)

=> s l14 and anti-IgE
L15 17 L14 AND ANTI-IGE

=> dup remove l15
PROCESSING COMPLETED FOR L15
L16 7 DUP REMOVE L15 (10 DUPLICATES REMOVED)

=> d l16 1-7 cbib abs

L16 ANSWER 1 OF 7 MEDLINE on STN DUPLICATE 1
2003126415. PubMed ID: 12639479. Synthetic IgE peptide vaccine for immunotherapy of allergy. Wang Chang Yi; Walfield Alan M; Fang Xinde; **Hammerberg Bruce**; Ye John; Li Ming Lie; Shen Fan; Shen Ming; Alexander Valerie; MacGlashan Donald W. (United Biomedical Inc., 25 Davids Drive, Hauppauge, NY 11788, USA.. cywang@unitedmedical.com) . Vaccine, (2003 Apr 2) 21 (15) 1580-90. Journal code: 8406899. ISSN: 0264-410X. Pub. country: Netherlands. Language: English.

AB An immunotherapeutic vaccine for allergy was produced by designing IgE-based synthetic peptide immunogens and selecting them for functional immunogenicity. The vaccine targets the binding site on IgE for the high affinity receptor Fc epsilon RI, by active immunization. The peptide target site on IgE heavy chain was selected from among the amino acid sequences for the C epsilon 2, C epsilon 3, and C epsilon 4 domains. These were characterised by epitope mapping studies for cross-reactivity to IgE and functional antigenicity. A peptide, modified from positions 413-435 of a loop region of C epsilon 3 and subjected to conformational constraint, elicited **anti-IgE** antibodies that blocked IgE-mediated histamine release. It was immunopotentiated by linkage to a promiscuous T helper site to produce a wholly synthetic chimaeric immunogen. This immunogen was shown to induce polyclonal site-specific **anti-IgE** antibodies that obstruct binding to Fc epsilon RI, inhibit histamine release by IgE-sensitised basophils, inhibit passive cutaneous anaphylaxis, and do not signal degranulation. Immunized dogs experienced significant reductions in total serum IgE.

L16 ANSWER 2 OF 7 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
2003:684513 The Genuine Article (R) Number: 707QY. Evaluation of the clinical and allergen specific serum immunoglobulin E responses to oral challenge with cornstarch, corn, soy and a soy hydrolysate diet in dogs with spontaneous food allergy. Jackson H A (Reprint); Jackson M W; Coblentz L; **Hammerberg B**. N Carolina State Univ, Dept Clin Sci, 4700 Hillsborough St, Raleigh, NC 27606 USA (Reprint); N Carolina State Univ, Dept Clin Sci, Raleigh, NC 27606 USA; Evesham Vet Clin, Marlton, NJ USA. VETERINARY DERMATOLOGY (AUG 2003) Vol. 14, No. 4, pp. 181-187. ISSN: 0959-4493. Publisher: BLACKWELL PUBLISHING LTD, 9600 GARSINGTON RD, OXFORD OX4 2DG, OXON, ENGLAND. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Fourteen dogs with known clinical hypersensitivity to soy and corn were maintained on a limited antigen diet and rice diet until cutaneous manifestations of pruritus were minimal (78 days). Sequential oral challenges with cornstarch, corn and soy were then performed. Subsequently, the dogs were fed a diet containing hydrolysed soy protein and cornstarch. Throughout the study period the dogs were examined for cutaneous manifestations of pruritus and, additionally, serum was collected for measurement of allergen-specific and total immunoglobulin (Ig)E concentrations. Intradermal testing with food antigens was performed prior to entry into the study and after 83 days. A statistically significant clinical improvement was measured between days 0 and 83. Significant pruritus was induced after oral challenge with cornstarch, corn and soy ($P=0.04$, 0.002 , 0.01 , respectively) but not with the hydrolysed diet ($P=0.5$). The positive predictive value of the skin test for soy and corn allergy was reduced after feeding a soy and corn free diet. Although increases in soy and corn-specific serum IgE concentrations were measured in individual dogs post challenge they were not statistically significant and could not be used to predict clinical hypersensitivity.

L16 ANSWER 3 OF 7 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
2002:724224 The Genuine Article (R) Number: 587ZJ. Evaluation of a spontaneous canine model of immunoglobulin E-mediated food hypersensitivity: Dynamic changes in serum and fecal allergen-specific immunoglobulin E values relative to dietary change. Jackson H A (Reprint); **Hammerberg B.** N Carolina State Univ, Coll Vet Med, Comparat Allergy Program, 4700 Hillsborough St, Raleigh, NC 27606 USA (Reprint); N Carolina State Univ, Coll Vet Med, Comparat Allergy Program, Raleigh, NC 27606 USA. COMPARATIVE MEDICINE (AUG 2002) Vol. 52, No. 4, pp. 316-321. ISSN: 1532-0820. Publisher: AMER ASSOC LABORATORY ANIMAL SCIENCE, 9190 CRESTWYN HILLS DR, MEMPHIS, TN 38125 USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The purpose of the pilot study reported here was to evaluate serum and fecal total and allergen-specific immunoglobulin E (IgE) responses to dietary change in five Maltese x beagle dogs with suspected food hypersensitivity, compared with those of five clinically normal dogs. Clinical parameters (pruritus, otitis, and diarrhea) improved in the Maltese x beagle dogs during feeding of a novel diet, and signs were exacerbated by oral allergen provocation. Relative concentrations of serum and fecal wheat-, corn-, and milk-specific IgE were determined by use of an ELISA. The onset of clinical signs of disease was accompanied by an increase in serum allergen-specific IgE concentrations. In contrast, changes in clinical signs of disease or allergen-specific IgE values were not seen in the control group undergoing the same regimen. Total serum IgE concentration was measured by use of the ELISA, and comparison with known quantities of a monoclonal IgE allowed absolute values to be reported. Values were high in the Maltese x beagle colony (7 to 34 $\mu\text{g/ml}$), compared with those in the control dogs (0.7 to 6 $\mu\text{g/ml}$). Total serum and total fecal IgE concentrations did not change in either group during the study. Although allergen-specific IgE was detected in the feces of both groups, significant interassay variability made interpretation of the results difficult. The authors concluded that these Maltese x beagle dogs satisfied the currently recognized clinical criteria for the diagnosis of canine food hypersensitivity. Furthermore, the clinical and serologic responses seen in these dogs in response to oral allergen provocation suggest that this may be a useful model for the study of spontaneous food hypersensitivity.

L16 ANSWER 4 OF 7 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
2002:429597 The Genuine Article (R) Number: 551HW. IgE is present on peripheral blood monocytes and B cells in normal dogs and dogs with atopic dermatitis but there is no correlation with serum IgE concentrations. Jackson H A (Reprint); Orton S M; **Hammerberg B.** N Carolina State

Univ, Comparat Allergy Program, 4700 Hillsborough St, Raleigh, NC 27606
USA (Reprint); N Carolina State Univ, Comparat Allergy Program, Raleigh,
NC 27606 USA. VETERINARY IMMUNOLOGY AND IMMUNOPATHOLOGY (MAR 2002) Vol.
85, No. 3-4, pp. 225-232. ISSN: 0165-2427. Publisher: ELSEVIER SCIENCE BV,
PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Blood was collected from 29 dogs, 14 with atopic dermatitis (AD) and 15 controls. Total serum IgE was quantitated. Peripheral blood monocytes were harvested and labeled with leucocyte markers and anti-canine IgE before analysis by flow cytometry. There was no statistically significant difference between the atopic and control groups when the mean number of cells in the monocyte (CD14), antigen presenting cell (CD1c) or B cell (CD21) populations were examined. However, the variation in cell numbers was significant and much greater in the atopic group for CD1c and CD14 labeled cells. The mean percentage of double labeled cells, CD1c/IgE and CD14/IgE was significantly lower in the atopic population compared with the controls. More variation was observed in the numbers of monocytes of atopic dogs (CD14/IgE) and antigen presenting cells (CD1c/IgE) of control dogs. The mean percentage of B cells expressing IgE was 65 and 51% in the atopic and control groups respectively which is greater than that reported in humans. There was no statistically significant difference. Total serum IgE concentrations were similar in each group and did not correlate with cell bound IgE in any of the leucocyte populations studied. Canine AD is associated with more variability in circulating monocyte numbers and lower numbers of monocytes expressing IgE than control dogs. Unlike in humans, there is no correlation between circulating and cell bound IgE. Furthermore, high levels of IgE in the dog may be related to a greater number of B cells in the circulation committed to IgE production. (C) 2002 Published by Elsevier Science B.V.

L16 ANSWER 5 OF 7 MEDLINE on STN DUPLICATE 2
2002120407. PubMed ID: 11844224. Skin mast cell histamine release following stem cell factor and high-affinity immunoglobulin E receptor cross-linking in dogs with atopic dermatitis. **Hammerberg B**; Olivry T; Orton S M. (Department of Microbiology, Pathology and Parasitology, College of Veterinary Medicine, North Carolina State University, Raleigh, NC 27606, USA.. bruce_hammerberg@ncsu.edu) . Veterinary dermatology, (2001 Dec) 12 (6) 339-46. Journal code: 9426187. ISSN: 0959-4493. Pub. country: England: United Kingdom. Language: English.
AB Stem cell factor (SCF) influences mast cell activation and inflammatory mediator release, and is elevated in tissues undergoing allergic inflammation. Wheal formation in response to the injection of SCF or anti-immunoglobulin (Ig)E antibody injection was compared between normal (n = 10) and nonlesional atopic (n = 10) canine skin. In situ SCF secretion was compared between lesional and nonlesional skin using immunohistochemistry. Histamine release by skin cell suspensions after stimulation with SCF, concanavalin A (ConA) or rabbit anticanine IgE antibodies was compared between normal and atopic dogs. All dogs exhibited strong responses to intradermal SCF injection at 10 and 50 ng mL(-1). Atopic dogs had significantly (P = 0.002) larger wheal responses to anti-IgE than normal dogs; but there was no difference in numbers of skin mast cells bearing IgE as detected by immunohistochemistry. Only atopic dogs exhibited interstitial deposition of SCF in both lesional and nonlesional skin specimens. Median histamine release stimulated by SCF in the absence of IgE from lesional skin cells was higher in atopic than normal dogs (P = 0.04). These experiments suggest that dermal SCF secretion could potentiate histamine release following IgE receptor cross-linking and thus, could be one of the explanations for the inherent mast cell hyperexcitability observed in canine atopic dermatitis.

L16 ANSWER 6 OF 7 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 3
2001:199714 Document No.: PREV200100199714. Naturally occurring canine IgG anti-IgE that binds IgE-bearing B cells but not IgE

bound to mast cells, isolated as a canine monoclonal antibody from a canine X mouse heterohybridoma. **Hammerberg, Bruce** [Reprint author]; Simkins, Steve [Reprint author]; Orton, Susan M. [Reprint author]. North Carolina State University, Raleigh, NC, USA. *Journal of Allergy and Clinical Immunology*, (February, 2001) Vol. 107, No. 2, pp. S272. print.

Meeting Info.: 57th Annual Meeting of the American Academy of Allergy, Asthma and Immunology. New Orleans, Louisiana, USA. March 16-21, 2001.

American Academy of Allergy Asthma and Immunology.

CODEN: JACIBY. ISSN: 0091-6749. Language: English.

L16 ANSWER 7 OF 7 MEDLINE on STN

DUPLICATE 4

1998194464. PubMed ID: 9533265. Auto IgG **anti-IgE** and IgG x IgE immune complex presence and effects on ELISA-based quantitation of IgE in canine atopic dermatitis, demodectic acariasis and helminthiasis. **Hammerberg B**; Bevier D; DeBoer D J; Olivry T; Orton S M; Gebhard D; Vaden S L. (Department of Microbiology, Pathology and Parasitology, College of Veterinary Medicine, North Carolina State University, Raleigh 27606, USA.) *Veterinary immunology and immunopathology*, (1997 Dec 12) 60 (1-2) 33-46. Journal code: 8002006. ISSN: 0165-2427. Pub. country: Netherlands. Language: English.

AB Atopic dermatitis is a common allergic disease manifestation in dogs; however, there is no correlation between clinical disease and detectable total serum IgE. Auto antibodies of the IgG subclass against IgE may affect the detection of serum IgE by immunoassay and may be important in the regulation of IgE production by B cells. ELISA were developed to detect serum antibodies specific for IgE using a newly available canine monoclonal IgE of known antigen specificity, generated from a canine x murine heterohybridoma. To test for correlation of auto IgG **anti-IgE** levels with manifestation of atopic dermatitis, the sera from 101 atopic dogs were compared with sera from non-atopic dogs of various breeds, foxhounds manifesting clinical signs of demodectic acariasis and helminth parasitized random bred dogs for quantities of IgG **anti-IgE** measured in units/ml compared to a high titer standard serum. To test for serum effects on quantitation of IgE, known amounts of canine monoclonal IgE were added to various sera and measured by capture ELISA with detecting monoclonal antibodies specific for heat labile or heat stabile epitopes. Unheated sera from dogs manifesting clinical atopic dermatitis and helminth parasitized dogs had levels of IgG **anti-IgE** that were significantly lower than various breeds of dogs not manifesting dermatologic lesions and foxhounds manifesting demodectic acariasis. Heating sera at 56 degrees C for 3 h to denature the high affinity binding site on the IgE heavy chain caused a marked increase over non-heated sera in detectable IgG **anti-IgE** in almost all dogs. This increase was most profound in helminth-infected dogs and foxhounds manifesting demodectic mange with 7 fold increases each, respectively, and in atopic dogs with a 5 fold increase compared to 3 fold increases for clinically-normal springer spaniels and all soft coated wheaten terriers. The terriers demonstrated an association of lower heated serum values of IgG **anti-IgE** with manifestation of a familial syndrome of protein-losing enteropathy and protein-losing nephropathy. The ability of mouse anti-canine IgE monoclonal antibodies specific for either heat labile or heat stabile epitopes to detect canine monoclonal IgE added to sera in known amounts varied from serum to serum and at different concentrations of the same serum, but did not correlate with IgG **anti-IgE** values for these sera. The range of absolute levels of serum IgE in dogs showing little or no inhibition of detection of added IgE was < 0.5 ng/micromilligram to 2 micrograms/micromilligram. It was concluded that the increase in detectable IgG **anti-IgE** after heating sera indicates that IgG x IgE immune complexes are normally present in most dogs; however, the increase over uncomplexed IgG **anti-IgE** was most pronounced in dogs manifesting atopic dermatitis and demodectic acariasis. A quantitative comparison of IgG **anti-IgE** or IgG x IgE to total serum IgE was not made

because the ability of monoclonal antibodies specific for either heat labile or heat stable epitopes on the IgE heavy chain to detect IgE added to serum, as well as innate serum IgE, was highly variable in different dilutions of serum from individual to individual.

=> s l14 and cat IgE
L17 0 L14 AND CAT IGE

=> s l14 and horse IgE
L18 0 L14 AND HORSE IGE

=> s l14 and "Ab 5.91"
L19 0 L14 AND "AB 5.91"

=> s l14 and "5.91 mAb"
L20 0 L14 AND "5.91 MAB"

=> s l14 and "5.91"
L21 0 L14 AND "5.91"

=> s l14 and "3.76"
L22 0 L14 AND "3.76"

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	157.48	157.69
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-5.84	-5.84

STN INTERNATIONAL LOGOFF AT 12:22:49 ON 14 DEC 2005